SEHSC | SILICONES ENVIRONMENTAL, HEALTH AND SAFETY COUNCIL of North America

January 16, 2001

Carol Browner
Administrator
US Environmental Protection Agency
PO Box 1473
Merrifield, VA 22116
Attn: Chemical Right-to-Know Program

Re: Response to EPA Comments on the SEHSC HPV Challenge Work Plan for Silane, [3-(2,3-epoxypropoxy) propyl] trimethoxy- (TMSPGE; CAS No. 2530-83-8)

Dear Administrator Browner:

In December 2000, the Silicones Environmental, Health and Safety Council (SEHSC) received EPA's comments on the test plan and supporting robust summaries for Silane, [3-(2,3-epoxypropoxy) propyl] trimethoxy- (TMSPGE; CAS No. 2530-83-8), which were submitted to EPA on July 20, 2000, as part of the SEHSC commitment to the HPV Challenge Program.

In reviewing the EPA comments, SEHSC's attention was caught by the statement on page 2 where the Agency recommended that a *"c) more thorough analysis of the structure-activity relationship of TMSPGE and siloxanes with reproductive toxicity (some organosiloxanes have been shown to cause reproductive effects in ma/e* Pharm., {*1972*}, *Vol. 21, and female [*Tox. Appl. Pharm., {*1972*}, *Vol 21, pp. 68-79] animals (organosiloxanes are among the expected hydrolysis/polymerization products of TMSPGE)), including the possible role of the epoxide in the TMSPGE, the reproductive effects observed with other siloxanes, and whether SIDS-level type tests would detect such effects."* SEHSC has reviewed the structure and reproductive toxicity of the substances described in the two *Toxicology and Applied Pharmacology* papers and has compared that with the structure/activity of TMSPGE. In this review, SEHSC found the following:

> As indicated in the July 20, 2000, HPV Challenge Work Plan, TMSPGE hydrolyzes and polymerizes, The polymerization product is a silsesquioxane, which is a complex siloxane resin structure connected via Si-0 bonds and exists as a mixture of polymeric species giving a range and distribution of molecular weights. The siloxanes described in the two *Toxicology and Applied Pharmacology* references are low molecular weight linear and cyclic siloxane oligomers containing phenylmethyl and dimethyl groups, The siloxanes that were reported to have relatively potent reproductive toxicity were the cyclic siloxanes containing phenylmethyl and dimethyl groups. Both TMSPGE and the resultant silsesquioxane are structurally distinct from and totally unlike the cyclic phenylmethyl- and dimethyl-containing cyclic siloxanes. Therefore, the use of structure-activity relationships as suggested by EPA is scientifically inappropriate for understanding the hazard potential of TMSPGE.

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SEHSC recognizes that EPA offered other recommendations in its December 2000 comments on the TMSPGE HPV Challenge Work Plan. As SEHSC scientists move forward with the testing commitment of TMSPGE, they will consider how these recommendations might further the goals of the voluntary HPV Challenge Program. SEHSC's HPV Challenge Registration Number is

Sincerely,

Reo Menning
Deputy Director